

Effect of *Convallaria majalis* on Kidney Function

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ABSTRACT

Objective: To evaluate the effect of *Convallaria majalis* on kidney function. The kidneys are vital organs that perform a variety of important functions in our body. Primary and secondary causes of kidney diseases produce changes in glomerular filtration rate that may leads to kidney failure. Blood parameters such as uric acid and creatinine are used to assess kidney function. *C. majalis* (CM) commonly called as Lily of the valley is a Homoeopathic remedy having valuable action on heart and also has diuretic action.

Methods: In the present study, the effect of CM was investigated on serum uric acid and creatinine, by administrating orally 70% alcoholic extract of CM (10 and 50 mg/kg), simvastatin (20 mg/kg), 0.05% dimethylsulphoxide (DMSO, 1ml/kg) and distilled water (1ml/kg) to test (A & B groups), positive, negative and control rabbits respectively for 14 days consecutively once in a day. On completion of trial, rabbits were sacrificed to collect blood and serum was separated to estimate uric acid and creatinine levels.

Results: Out of two tested doses, 10 mg/kg of CM produced significant decrease in uric acid levels from 10.97-8.40 mg/dL in test rabbits (Test A) when compared with control, negative & positive control groups ($p < 0.05$). However, the same dose of extract showed no effect on serum creatinine levels. Whereas alcoholic extract @ 50 mg/kg was found ineffective in reducing either of serum uric acid and creatinine levels.

Conclusion: According to the data, alcoholic extract of CM @ 10mg/kg was found as a significant hypouricemic agent.

Key words: Glomerular filtration, kidney, uric acid, creatinine, hypouricemic activity.

INTRODUCTION

The kidneys are vital organs that perform a variety of important functions in our body.¹ Diseases of the kidneys produce changes in glomerular filtration rate (GFR) that may leads to kidney failure.¹ Chronic kidney disease (CKD) is a worldwide public health problem increasing day by day.² In the United States alone, an estimated 26 million people suffer from CKD.² The number of persons with kidney failure who are treated with dialysis and transplantation is projected to increase from 340,000 in 1999 to 651,000 in 2010.³ Many

developing countries are facing a silent epidemic of CKD.⁴ Outcomes of CKD include not only progression to kidney failure but also complications of reduced kidney function and increased risk of cardiovascular disease and all-cause mortality overall. There is convincing evidence that CKD can be prevented or its progression can be delayed, if effective management is initiated in time. Hence, identifying patients with CKD and providing prompt intervention play an important role in appropriate management of CKD.⁵ Disturbances in mineral metabolism and bone disease are common complications of CKD and an important cause of morbidity and decreased quality of life.⁶

There are few well-established risk factors for developing CKD including age, GFR, hematuria, hypertension, diabetes, serum lipids (atherosclerosis), obesity, physical inactivity, smoking status, and consumption of alcohol.⁷⁻⁸ Out of these, diabetes and hypertension are strong predictors for the development and progression of CKD.⁸ The initial conventional treatments of CKD is to control the disease that causing it to slowing down the disease progression and

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improving the outcomes by keeping the glycosylated hemoglobin (Hb A1C) level less than 7 and using angiotensin converting enzyme (ACE) inhibitors, angiotensin-II receptor antagonist, statin, diuretics or drugs that alter the excretion of organic molecules like probenecid, sulfapyrazone, etc but in severe cases dialysis and transplantation must be recommended.⁹⁻¹⁰ Other studies have also reported that physical activity has been associated with a lower rate of nephropathy and renal dysfunction.⁷ In homeopathic system of medicine, many plant-based drugs are also used for the treatment of kidney diseases having diuretic effect like *Berberis Vulgaris*, *Belladonna*, and *Aconite* etc.¹¹

In the present study *Convallaria majalis*, commonly known as lily of the valley (family: *Ruscaceae*) is a well known homeopathic medicine having antispasmodic, cardiogenic, strongly diuretic, emetic, febrifuge, laxative and sedative effects.¹²⁻¹³ Even though it has strong diuretic effect but its effect on serum uric acid and creatinine has not been investigated yet. Therefore, the present study was designed to investigate the effect of *C. majalis* (CM) on serum uric acid and creatinine, both of these are considered as biomarkers of kidney dysfunction.¹⁴

MATERIALS AND METHODS

Animals

Rabbits weighing 1-1.5 kg were purchased from local supplier of Jinnah University for Women. The animals were kept under hygienic conditions with standard laboratory diet and water *ad libitum*.

Convallaria majalis

Alcoholic (70%) mother tincture of *C. majalis* (Schwabe, Germany) was purchased from authentic homeopathic dealer Saddar, Karachi.

Simvastatin

Simvastatin with brand name limitrol purchased from PharmEvo (Pvt.) Ltd, Pakistan and used as positive control in a dose of 20mg/kg.

Dimethylsulphoxide (DMSO)

Analytical reagent grade DMSO was purchased from Fisher Scientific (UK) and its 0.05% concentration in distilled water was used as vehicle for administering the doses of alcoholic extract of *C. majalis* in experimental test rabbits.

Preparation of alcoholic extract of *C. majalis*

The alcoholic (70%) mother tincture of the *C. majalis* was subjected to evaporate by using rotary vacuum evaporator to obtain brown residue and considered as alcoholic extract.

Study Protocol

Experimental rabbits were divided into different groups including control, negative & positive controls and test groups. Each group contains 6 rabbits. The control, negative & positive controls were treated orally with 1ml of each of distilled water, DMSO (0.05%), simvastatin (20mg/kg) respectively once in a day and consecutively for 14 days. Whereas test group was further sub-divided into two groups including test A & B, which were treated with alcoholic extract of *C. majalis* in doses of 10 and 50 mg/kg respectively once in a day orally for the same period. On completion of trial, rabbits were sacrificed and blood was collected from each group to separate serum which was used to analyze biochemical parameters on Spectro UV-Visible Auto, PC Scanning Spectro-photometer, Labomed, Inc.

Biochemical Analysis

Uric acid and creatinine were determined by commercially available enzymatic kits (Randox).

Statistical Analysis

The data were analyzed by Student's *t*-test (Graphpad software, Quick calcs Online calculators for Scientists)¹⁵ and the differences were found significant when $p < 0.05$. Values are expressed as Mean \pm SD.

RESULTS

A significant decrease ($p < 0.05$) was observed in the level of uric acid upto 8.40 mg/dL in test rabbits treated orally with CM @ 10 mg/kg for 14 days as compared to second dose of same alcoholic extract @ 50 mg/kg. The uric acid levels in control rabbits treated with distilled water (1ml/kg), negative control treated with 0.05% DMSO (1ml/kg) and positive control treated with simvastatin (20mg/kg) were found as 10.96, 10.10 and 10.10 mg/dL respectively (Table I, Figure 1). The serum creatinine level was found as 2.13 mg/dL in test group (Test A) treated with alcoholic extract of CM @ 10 mg/kg which was almost same to its level found in control group. Whereas CM @ 50 mg/kg showed increase in serum creatinine level (Table I).

DISCUSSION

Chronic kidney disease is a worldwide public health problem.² Morbidity and mortality associated with kidney failure is increasing day by day. Kidney diseases can be prevented and its progression can be delayed if it is diagnosed effectively and managed in time.⁵ Glomerular filtration rate (GFR) is considered as best indicator of renal function in both health and disease states.¹⁶ Besides this in clinical practice, serum creatinine, uric acid and urea are also considered as biomarkers of renal function.¹⁷⁻¹⁸ Out of these, the concentration of urea can be affected by high protein diet.⁹ Usually the increase in serum uric acid and creatinine indicates physician that patient is suffering from kidney dysfunction.¹⁹ Evidence suggested that herbal, homoeopathic and allopathic medicinal systems are quite beneficial in the treatment of kidney diseases.^{9,11} *C. majalis* (CM) which is already reported as strong diuretic agent besides being antihypertensive agent¹²⁻¹³ was selected to determine its effect on serum uric acid and creatinine levels in experimental rabbits. Where, the alcoholic extract of CM @ 10 mg/kg was found to have significant hypouricemic effect ($p < 0.05$) as compare to dose @ 50 mg/kg of same extract. The alcoholic extract @ 10 mg/kg produced a pronounced fall in serum uric acid level up to 8.40 mg/dL in test rabbits (Test A) treated orally once in a day for 14 days consecutively as compare to control, negative and positive control groups which showed serum uric acid levels ranging from 10.10 - 10.96 mg/dL. The serum creatinine levels were found almost same in control, positive control and test group (test A) that treated with alcoholic extract @ 10 mg/kg. However, alcoholic extract @ 50 mg/kg induce an increase in serum creatinine level of test group (Test B).

On the basis of results it has been concluded that alcoholic extract of *C. majalis* at a dose 10 mg/kg was found to be effective in reducing or improving serum uric acid level, hence preventing chronic kidney disease. The possible mechanisms of action of hypouricemic effect of CM might be direct and compatible to the actions of primary uricosuric drugs such as either by inhibiting the reabsorption of uric acid in proximal²⁰ and distal convoluted tubules²¹ or by inhibiting the activity of xanthine oxidase, one of the rate-regulatory enzymes in uric acid formation thus reducing the synthesis of uric acid²² or indirect and similar to secondary uricosuric drugs such as amlodipine, statins, fenofibrate, etc.²³ However the work is still in progress to evaluate its effect on kidney disease and to determine its exact mechanism of action in reducing serum uric acid.

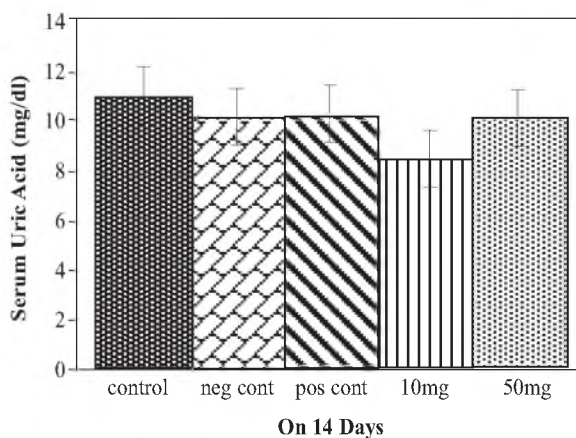
Table I: Effect of alcoholic extract of *C. majalis* on serum uric acid and creatinine

Groups	Uric Acid (mg/dL)	Creatinine (mg/dL)
Control (Dist. Water 1ml/kg)	10.96±0.85	2.86±2.13
Negative Control (0.05% DMSO 1ml/kg)	10.10±0.75	3.46±0.46
Positive Control (Simvastatin 20mg/kg)	10.10±0.45	2.20±1.11
Test A (<i>C. majalis</i> @ 10 mg/kg)	8.40±0.95*	2.13±1.13
Test B (<i>C. majalis</i> @ 50 mg/kg)	10.03±0.75	5.35±5.77

Each value is the mean ± SD (n = 6). * = $p < 0.05$, * = $p < 0.05$ represent significant when compared with control, negative & positive controls.

FIGURE I

Comparative study of serum uric acid (mg/dL) in control, negative & positive control and test groups (A & B) treated with distilled water (1ml/kg), 0.05% DMSO (1 ml/kg), simvastatin (20mg/kg) & alcoholic extract of *C. majalis* (10 & 50 mg/kg) respectively. Each value expressed as mean ± SD (n= 6)



* = $p < 0.05$ represent significant differences from respective control

CONCLUSION

The obtained result of present study concluded that only small dose (concentration) of alcoholic extract of *C. majalis* was found as a significant hypouricemic agent.

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